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AMENDMENTS TO THE CLAIMS

(Currently amended) A compound of formula I:

or a pharmaceutically acceptable salt thereof, wherein:

R1 is halogen, CN, NO2, or VmR;

Z¹ and Z³ are each independently CR^Z;

 Z^2 is CR^1 ;

each occurrence of R^Z is independently halogen, CN, NO₂, or U_nR^* ; R^2 is U_nR^* :

each occurrence of R⁴ is independently halogen, CN, NO₂, or V_mR;

each occurrence of U or V is independently an optionally substituted C_{1.6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by –NR-, -S-, -O-, -CS-, [[-CO₂-,]] -OCO-, [[-CO-,]] -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂-, -CONRN-, -SO₂-, -CONRN-, -SO₂-, -CONRN-, -SO₂-, -CONRN-, -NRSO₂-, -

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m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

O1 is -CO-:

 R^3 is Q^2 -Ar¹, wherein Q^2 is -(CHR⁶)_q-, where q is 1, 2, or 3,

or R2 and Q1-R3, taken together with the intervening nitrogen atom, form the cyclic

group: $Y = \{Y\}_s$, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -SO₂-, -O-, -S-, -NR⁵-, or -C(R⁵)₂-, and R⁵ is

U_nR';

 Q^3 is a bond or a $C_{1.6}$ alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -COCO-, -CONR'-, -NR'CO₂-, -NR'CO₂-, -SO₂NR'-, -NR'SO₂-, -CONR'NR'-, -NR'CONR'-, -NR'NR'-, -NR'SO₂NR'-, -SO-, or -SO₂-; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of R^6 , wherein each occurrence of R^6 is independently halogen, CN, NO₂, or U_nR' , or two occurrences of R^6 , or R' and R^6 , taken together with the atoms to which

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they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; and

Ar¹ is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from oxygen or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from oxygen or sulfur; wherein Ar¹ is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -CO₂-, -COC-, -COC-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-;

Ar² is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar² is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -CO₂-, -OCO-.

-CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-,
-NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-; [[and]]
each occurrence of R⁷ is independently R*, halogen, NO₂, or CN:

cach of the optional substituents of said aryl or heteroaryl ring is selected from halogen; -R°; -OR°; -SR°; phenyl optionally substituted with R°; -O(phenyl), optionally substituted with R°; -CH=CH(phenyl), optionally substituted with R°; -CH=CH(phenyl), optionally substituted with R°; -NO; -CN; -N(R°); -NR°C(O)R°; -NR°C(S)R°; -NR°C(O)N(R°); -NR°C(S)N(R°); -NR°C(O)R°;

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-NR°NR°C(O)N(R°)₂; -NR°NR°CO₂R°; -C(O)C(O)R°; -C(O)CH₂C(O)R°; -CO₂R°; -C(O)R°; -CO₂R°; -C(O)R(R°)₂; -C(O)N(R°)₂; -C(O)N(R°)₂; -C(O)N(R°)₂; -C(O)N(R°)₂; -C(O)N(R°)₂; -C(O)N(R°)₂; -C(O)N(R°)₂; -C(O)N(R°)₂; -NR°SO₂N(R°)₂; -NR°SO₂

each of the optional substituents on said alkylidene chain, aliphatic, cycloalkyl, or heterocyclyl is selected from the list of optional substituents of optional substituents for aryl and heteroaryl rings and further comprise =O, =S, =NNHR*, =NN(R*)₂, =NNHC(O)R*, =NNHCO₂(alkyl), =NNHSO₂(alkyl), or =NR*, where each R* is independently selected from hydrogen or a C₁₋₆ aliphatic group;

provided that:

for compounds having the structure:

R³ is not any one of the following groups: -CH₂(3-NHCOPh-phenyl), -CH₂-pyrrolidine, unsubstituted benzyl, -CH₂-naphthyl, -CH₂CH₂-3-(4-Cl-phenyl)-1-phenyl-1-H-pyrazol-4-yl, or -CH₃(1,3-dioxoisoindole).

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2-3. (Canceled)

- 4. (Previously presented) The compound of claim 1, wherein \mathbb{R}^2 is hydrogen, or is $U_n\mathbb{R}^2$, where n is 1, and U is a $C_{1.6}$ alkylidene chain wherein one or two methylene units are optionally and independently replaced by O, NR, S, or C(O).
- 5. (Previously presented) The compound of claim 1, wherein U is -CH₂C, -CH₂CH₂-, -CH₂-, -

6-7. (Canceled)

(Previously presented) The compound of claim 1, wherein R⁶ is CH₂OH,
 CH₂CH₂OH, OH, OMe, OEt, NH₂, NH(Me), NH(Et), N(Me)(Me), CH₂NH₂,
 CH₂CH₂NH₂, NHCO₂t-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl,
 NH(CH₂)₃NH₂, NH(CH₂)₂NH₂, NH(CH₂)₂NHEt, NHCH₂pyridyl, NHSO₂phenyl,
 NHC(O)CH₂C(O)Ot-butyl, NHC(O)CH₂NH₃, and NHCH₂-imidazol-4-yl.

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(Previously presented) The compound of claim 3, wherein Ar¹ is:

a e i k

$$t cc ee$$

$$(TR^{7})_{k} (TR^{7})_{k} (TR^{7})_{k}$$

$$i jj kk$$

wherein t is 0, 1, 2, 3, 4 or 5, and wherein any Ar^1 is bonded to Q^2 through any substitutable carbon atom, and wherein one or more hydrogen atoms on any substitutable carbon atom is substituted with one or more independent occurrences of TR².

- (Previously presented) The compound of claim 9, wherein Ar¹ is a, e, i, k, cc, jj, or pp.
- 11. (Original) The compound of claim 9, wherein T is a bond or is an optionally substituted C_{1.6} alkylidene chain wherein one or two methylene units are optionally and

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independently replaced by -O-, -NR-, -S-, -SO₂-, -COO-, -CO-, -OSO₂-, -NRSO₂, -CONR-, or -SO₂NR-, and \mathbb{R}^7 is R' or halogen.

12. (Original) The compound of claim 9, wherein each occurrence of TR⁷ is independently -C₁₋₃alkyl, -OR', -SR', -CF₃, -OCF₃, -SCF₃, -F, -Cl, I, -Br, -COOR', -COR', -O(CH₂)₄N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)₃CON(R)(R'), -O(CH₂)₃CON(R)(R'), -O(CH₂)₂CON(R)(R'), -C(CH₂)₃OR', -(CH₂)₂OR', -CH₂OR', optionally substituted phenyl or benzyl, -N(R)(R'), -(CH₂)₄N(R)(R'), -(CH₂)₃N(R)(R'), -(CH₂)₂N(R)(R'), -(CH₂)₂N(R)(R'), or SO₂N(R)(R'), NRSO₂R', CON(R)(R'), or -OSO₂R'.

13. (Canceled)

- 14. (Previously presented) The compound of claim 1, wherein Q^3 is a direct bond, or is -(CHR 6) $_q$ 7, -(CHR 6) $_q$ 0, -(CHR 6) $_q$ 5, -(CHR 6) $_q$ 5, -(CHR 6) $_q$ 5(O)-, -(CHR 6) $_q$ 7, -(CH 6) $_q$ 7, -NR(CH $_2$) $_{1-4</sub>N(R)(R^3)$, -NR(CH $_2$) $_{1-4</sub>N(R)(R^3)$, -NR(CH $_2$) $_{1-4}$ 8, -NR(CH $_2$) $_{1-4}$ 9, or two occurrences of R^6 , taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring.
- 15. (Original) The compound of claim 14, wherein R⁶ is CH₂OH, CH₂CH₂OH, OH, OMe, OEt, NH₂, NH(Me), NH(Et), N(Me)(Me), CH₂NH₂, CH₂CH₂NH₂, NHCO₂t-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, NH(CH₂)₃NH₂, NH(CH₂)₂NHEt, NHCH₂pyridyl, NHSO₂phenyl, NHC(O)CH₂C(O)Ot-butyl, NHC(O)CH₃NH₃, and NHCH₂-imidazol-4-vl.

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16. (Previously presented) The compound of claim 1, wherein Ar² is:

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wherein t is 0, 1, 2, 3, 4 or 5, and wherein any Ar^2 is bonded to Q^3 through any substitutable nitrogen or carbon atom, and wherein one or more hydrogen atoms on any substitutable nitrogen or carbon atom is substituted with one or more independent occurrences of TR^7 .

- 17. (Original) The compound of claim 16, wherein Ar² is a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll, or pp.
- 18. (Original) The compound of claim 16, wherein T is a bond or is an optionally substituted C₁₋₆ alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, -SO₂-, -COO-, -CO-, -OSO₂-, -NRSO₂, -CONR-, or -SO₂NR-, and R⁷ is R' or halogen.

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(Previously presented) The compound of claim 1, wherein R⁵ is hydrogen,
 (CH₂)₂OR', (CH₂)₂OR', (CH₂)OR', (CH₂)₃N(R')₂, (CH₂)₂N(R')₂, (CH₂)N(R')₂, or C₁₋₄aliphatic.

21-22. (Canceled)

- (Original) The compound of claim 1, wherein each occurrence of R¹ is independently hydrogen, halogen, optionally substituted C₁-C₄aliphatic, OR, SR, or N(R).
- (Previously presented) The compound of claim 23, wherein each occurrence of R¹ is independently hydrogen, halogen, -CH₃, -CH₂CH₃, -OH, -OCH₃, -SCH₃, -NH₂, -N(CH₃)₂, -N(CH₂CH₃)₂, -NH(CH₂)₂NHCH₃, -NH(cyclopropyl), -NH(CH₂)₂cyclopropyl, or -NH(CH₂)₂N(CH₃)₂.
- (Original) The compound of claim 1, wherein each occurrence of R^Z is independently hydrogen, halogen, C₁-C₄aliphatic, OH, OR', or N(R)(R').
- 26. (Original) The compound of claim 25, wherein each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH₂, or N(Me)₂.
- (Currently amended) The compound of claim 1, wherein R⁴ groups are each
 independently hydrogen, C₁₋₆aliphatic, CN, COR, C(=O)N(R)₂, or halogen.

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28. (Previously presented) The compound of claim 1, wherein one occurrence of R⁴ is CN and compounds have the general structure II-a:

 (Previously presented) The compound of claim 1, wherein R⁴ is hydrogen and compounds have the general structure III-a;

30. (Canceled)

31. (Previously presented) The compound of claim 1, wherein R⁴ is hydrogen and compounds have the general structure VII-a:

(Canceled)

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33. (Previously presented) The compound of claim 1, wherein R⁴ is hydrogen and compounds have the general structure XI-a;

34. (Previously presented) The compound of claim 9, wherein Q^1 is -CO-, Q^2 is CHR⁶, q is 1 2, or 3, and compounds have one of formulas XIV, XV, or XVI:

$$R^1$$
 R^2
 R^4
 R^2
 R^6
 R^4
 R^2
 R^6
 R^6
 R^7
 R^7
 R^7
 R^7
 R^7
 R^7

35. (Previously presented) The compound of claim 9, wherein Q^1 is -CO-, Q^2 is CHR⁶, q is 1, 2 or 3, and compounds have one of formulas XVII, XVIII, or XIX:

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- 36. (Previously presented) The compound of claims 34 or 35, wherein compound variables are selected from one of more of the following groups:
- a) each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OR, SR, or $N(R)_2$;

b) each occurrence of R¹ is independently hydrogen, halogen, -CH₃, -CH₂CH₃,
-OH, -OCH₃, -SCH₃, -N(CH₃)₂, -N(CH₂CH₃)₂, -N(CH₂)₂NH(CH₂)₂NHCH₃,
-NH(cyclopropyl), -NH(CH₂)₂cyclopropyl, or -NH(CH₃)₂N(CH₃)₂;

c) each occurrence of R^Z is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OH, O(R'), or N(R)(R');

d) each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH2, or N(Me):

e) R² is hydrogen, or is U₃R², where n is 1, and U is–CH₂-, -CH₂CH₂-,
-CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂-,
-CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂-,
-CH₂CH₃S-, -CH₂CH₂NR-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂-,
-CH₂CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH₂CH₂CH₂-,
-CH₂CH₂CH₂-, -(CH₂)ANHCH₂-, -(CH₂)ANHCH₂CH₂-, or

-CH₂CH₂NHCH₂CH₂-, and R' groups are hydrogen, C₁-C₄alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R', taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring;

 f) each occurrence of R⁴ is independently hydrogen, C₁₋₆aliphatic, CN, COR, COOR, CON(R)₂, or halogen;

g) q is 1, 2, or 3;

h) R^6 is R', -N(R)(R'), - $(CH_2)_{1-4}N(R)(R')$, -OR', - $(CH_2)_{1-4}OR'$, - $NR(CH_2)_{1-4}$, -4N(R)(R'), - $NR(CH_2)_{1-4}SO_2R'$, - $NR(CH_2)_{1-4}COOR'$, or - $NR(CH_2)_{1-4}COR'$, or two occurrences of R^6 , taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated rine:

i) R⁶ is CH₂OH, CH₂CH₂OH, OH, OMe, OEt, NH₂, NH(Me), NH(Et),
N(Me)(Me), CH₂NH₂, CH₂CH₂NH₂, NHCO₂t-butyl, phenyl, cyclopentyl, methyl, ethyl,
isopropyl, cyclopropyl, NH(CH₂)₃NH₂, NH(CH₂)₂NH₂, NH(CH₂)₂NHEt, NHCH₂-pyridyl,
NHSO₂-phenyl, NHC(O)CH₂C(O)O₇-butyl, NHC(O)CH₃NH₃, and NHCH₂-imidazol-4-yl;

- j) Ar^1 is ring $\bf a, e, i, k, ce, jj$, or $\bf pp$ wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted $C_{1.6}$ alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, $-SO_2$ -, -COO-, -CO-, $-OSO_2$ -, $-NRSO_2$ -, -CONR-, or
- -SO₂NR-, and R⁷ is R' or halogen; or
- k) Ar¹ is ring **a**, **e**, **i**, **k**, **ec**, **jj**, or **pp** wherein t is 0, 1, 2, or 3, and each occurrence of TR⁷ is independently -C_{1,3}alkyl, -OR', -SR', -CF₃, -OCF₃, -SCF₃, -F, -Cl, I, -Br, -COOR', -COR', -O(CH₂)₄N(R)(R'), -O(CH₂)₅N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)₂N(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)₂CON(R)(R'), -C(CH₂)₂ON', -(CH₂)₄ON', -(CH₂)₄ON', -(CH₂)₄ON', -(CH₂)₄N(R)(R'), -(CH₂)₅N(R)(R'), -(CH₂)₅

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-(CH₂)₂N(R)(R'), -(CH₂)N(R)(R'), -SO₂N(R)(R'), -NRSO₂R', -CON(R)(R'), or -OSO₂R'.

37. (Currently amended) The compound of claim 34 or 35, q is 1, and Ar¹ is optionally substituted phenyl and compounds of general formula XIV-A through XIX-A are provided:

wherein:

each occurrence of R1 is hydrogen;

each occurrence of RZ is hydrogen;

 R^2 is hydrogen, or is U_nR ', where n is 1, and U is- CH_2 -, - CH_2CH_2 -,

-CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH₂O-, -CH₂S-, -CH₂NR-, -CH₂CH₂O-,
-CH₂CH₂S-, -CH₂CH₂NR-, -CH₂CH₂CH₂O-, -CH₂CH₂CH₂S-, -CH₂CH₂CH₂NR-,
-CH₂CH₂CH₂O-, -CH₂CH₂CH₂CH₂S-, -CH₂CH₂CH₂NR-, -CH₂CH₂OCH₂CH₂C-,
-(CH₂)₄NHCH₂-, -(CH₂)₃NHCH₂CH₂-, or -CH₂CH₂NHCH₂CH₂-, and R' groups are
hydrogen, C₁-C₄alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R',
taken together with the nitrogen atom to which they are bound, form an optionally
substituted 5- or 6-membered heterocyclyl rine:

each occurrence of R⁴ is independently hydrogen, C₁₋₆aliphatic, CN, COR, COOR, CON(R)₂, or halogen;

 $R^6 \text{ is } R', -N(R)(R'), -(CH_2)_{1-4}N(R)(R'), -OR', -(CH_2)_{1-4}OR', \\ -NR(CH_2)_{1-4}N(R)(R'), -NR(CH_2)_{1-4}SO_2R', -NR(CH_2)_{1-4}COOR', \text{ or } \\ -NR(CH_2)_{1-4}COR'; \text{ and } \\$

$$\label{eq:tison} \begin{split} t \ is \ 0, 1, 2, or \ 3, \ and \ each \ occurrence \ of \ TR^7 \ is \ independently \ -C_{1-3}alkyl, \ -OR^7, \\ -SR^7, -CF_3, -OCF_3, -SCF_3, -F, -Cl, I, -Br, -COOR^7, -COR^7, -O(CH_2)_4N(R)(R^7), \\ -O(CH_2)_3N(R)(R^7), -O(CH_2)_2N(R)(R^7), -O(CH_2)N(R)(R^7), -O(CH_2)_4CON(R)(R^7), \\ -O(CH_2)_3CON(R)(R^7), -O(CH_2)_2CON(R)(R^7), -O(CH_2)CON(R)(R^7), -C(O)N(R)(R^7), \\ -(CH_2)_4OR^7, -(CH_2)_3OR^7, -(CH_2)_2OR^7, -CH_2OR^7, \ optionally \ substituted \ phenyl \ or \ benzyl, -N(R)(R^7), -(CH_2)_4N(R)(R^7), -(CH_2)_3N(R)(R^7), -(CH_2)_2N(R)(R^7), \\ -(CH_2)N(R)(R^7), -SO_2N(R)(R^7), -NRSO_2R^7, -CON(R)(R^7), \ or \ -OSO_2R^7. \end{split}$$

38. (Previously presented) The compound of claim 16, wherein R² and Q¹-R³, taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula XX through XXV:

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39. (Previously presented) The compound of claim 16, R² and Q¹-R³, taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula XXVI through XXXI:

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40. (Previously presented) The compound of claim 16, wherein R² and Q¹-R³, taken together with the atoms to which they are bound form a 6-membered cyclic group, and compounds have the general formula XXXII through XXXVII:

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wherein W is O, NR5, or CHR5.

- 41. (Original) The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:
- a) each occurrence of R¹ is independently hydrogen, halogen, optionally substituted C₁-C₄aliphatic, OR, SR, or N(R):
- b) each occurrence of R^Z is independently hydrogen, halogen, optionally substituted C_1 - C_4 aliphatic, OH, OR' or N(R)(R');
- c) each occurrence of R^4 is independently hydrogen, $C_{1.6}$ aliphatic, CN, COR, COOR, CON(R)₂, or halogen;
- d) R⁵ is hydrogen, (CH₂)₃OR', (CH₂)₂OR', (CH₂)OR', (CH₂)₂N(R')₂, (CH₂)₂N(R')₂, (CH₂)N(R')₂, or C₁₋₄aliphatic;
- e) Q^3 is a direct bond, or is -(CHR⁶) $_q$ -, -(CHR⁶) $_q$ O-, -(CHR⁶) $_q$ S-, -(CHR⁶) $_q$ S(O)-, -(CHR⁶) $_q$ S(O)-, -(CHR⁶) $_q$ NR-, or -(CHR⁶) $_q$ C(O)-, wherein q is 0, 1, 2, or 3; and
- f) Ar² is ring **a**, **b**, **e**, **g**, **h**, **i**, **j**, **k**, **n**, **r**, **ce**, **dd**, **ff**, **jj**, **ll**, or **pp**, wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted C₁₋₆ alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, -SO₂-, -COO-, -CO-, -OSO₂-, -NRSO₂, -CONR-, or -SO₂NR-, and R⁷ is R¹ or halogen.

42. (Currently amended) The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:

- a) each occurrence of R¹ is independently hydrogen, halogen, -CH₂, -CH₂CH₃,
 -OH, -OCH₃, -SCH₃, -NH₂, -N(CH₃)₂, -N(CH₂CH₃)₂, NH(CH₂)₂NHCH₃,
 NH(evelopropyl), NH(CH₂)₂velopropyl, or NH(CH₂)₂N(CH₃):
- b) each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH2, or N(Me):
- e) each occurrence of R^4 is independently hydrogen, C_{1-6} aliphatic, CN, COR_{7} $CON(R)_2$, or halogen;
- $\label{eq:ch22} \begin{array}{l} d) \ R^5 \ is \ hydrogen, \ (CH_2)_3OR', \ (CH_2)_2OR', \ (CH_2)OR', \ (CH_2)_3N(R')_2, \\ (CH_2)_2N(R')_2, \ (CH_2)N(R')_2, \ c \ C_{14} a liphatic; \end{array}$
- e) Q^3 is a direct bond, or is -(CHR 6) $_q$ r, -(CHR 6) $_q$ O-, -(CHR 6) $_q$ S-, -(CHR 6) $_q$ S(O) $_2$ -, -(CHR 6) $_q$ NO-, -(CHR 6) $_q$ NR-, or -(CHR 6) $_q$ C(O)-, wherein q is 0, 1, 2, or 3; and

f) Ar² is ring a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll, or pp, wherein t is 0, 1, 2, or 3, and each occurrence of TR⁷ is independently -C_{1,3}alkyl, -OR³, -SR³, -CF₃, -CF₃, -CCF₃, -F, -Cl, I, -Br, -COOR³, -COR³, -O(CH₂)₄N(R)(R³),

- $-O(CH_2)_3N(R)(R'), -O(CH_2)_2N(R)(R'), -O(CH_2)N(R)(R'), -O(CH_2)_4CON(R)(R'), \\$
- -O(CH₂)₃CON(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)₂CON(R)(R'), -C(O)N(R)(R'), -(CH₂)₄OR', -(CH₂)₃OR', -(CH₂)₂OR', -CH₂OR', optionally substituted phenyl or benzyl, -N(R)(R'), -(CH₂)₄N(R)(R'), -(CH₂)₂N(R)(R'), -(CH₂)₂N(R)(R'), -(CH₂)N(R)(R'), -SO₂N(R)(R'), -NRSO₂R', -CON(R)(R'), or -OSO₂R'.
- 43. (Previously presented) The compound of claims 38, 39 or 40, wherein Ar² is optionally substituted phenyl and compounds of general formula XX-A, through XXXVII are provided:

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XXVII-A

XXVI-A

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XXVIII-A

$$(TR^{7})_{1}$$
 R^{1}
 R^{2}
 R^{2}
 R^{5}
 R^{5}
 R^{5}

XXX-A

XXXII-A

XXXIII-A

XXXIV-A

XXXV-A

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44. (Currently amended) The compound of claim 43, wherein compound variables are selected from:

each occurrence of R1 is hydrogen;

each occurrence of RZ is hydrogen;

each occurrence of R⁴ is independently hydrogen, C₁₋₆aliphatic, CN, COR,

COOR, CON(R)2, or halogen;

 $R^{5} \text{ is hydrogen, } (CH_{2})_{3}OR', (CH_{2})_{2}OR', (CH_{2})OR', (CH_{2})_{3}N(R')_{2}, (CH_{2})_{2}N(R')_{2}, \\ (CH_{2})N(R')_{2}, \text{ or } C_{14} \\ \text{aliphatic;}$

 Q^3 is a direct bond, or is -(CHR⁶) $_q$ -, -(CHR⁶) $_q$ -, -(CHR⁶) $_q$ -S, -(CHR⁶) $_q$ S(O)-, -(CHR⁶) $_q$ NR-, or -(CHR⁶) $_q$ C(O)-, wherein q is 0, 1, 2, or 3; and t is 0, 1, 2, or 3, and each occurrence of TR⁷ is independently -C_{1.3}alkyl, -OR',

-SR', -CF₃, -OCF₃, -SCF₃, -F, -Cl, I, -Br, -COOR', -COR', -O(CH₂)₄N(R)(R'),

 $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$,

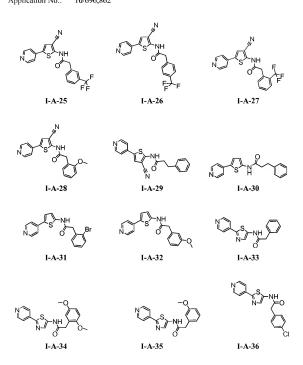
-O(CH₂)₃CON(R)(R'), -O(CH₂)₂CON(R)(R'), -O(CH₂)CON(R)(R'), -C(O)N(R)(R'),

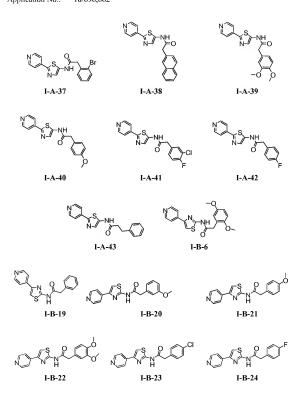
-(CH₂)₄OR', -(CH₂)₃OR', -(CH₂)₂OR', -CH₂OR', optionally substituted phenyl or benzyl, -N(R)(R'), -(CH₂)₄N(R)(R'), -(CH₂)₃N(R)(R'), -(CH₂)₂N(R)(R'),

-(CH₂)N(R)(R'), -SO₂N(R)(R'), -NRSO₂R', -CON(R)(R'), or -OSO₂R'.

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45. (Currently amended) The compound of claim 1, having one of the structures:





N N N H Br	I-B-26	N NH OCI CI
S NH CI	S NH CI CI I-B-29	N NH NH NH2 1-B-30
N-N-NH NH ₂ CI I-B-31	I-B-32	I-B-33
SNH N-N-N-1-B-34	I-B-35	NH CI
1-10-34	1-15-33	I-D-30

S NH CI	I-B-38	I-B-39
I-B-40	I-B-41	I-B-42
I-B-43	I-B-44	I-B-45
N N N N N N N N N N N N N N N N N N N	S NH F	NH NH FE F
NH NH OH	I-B-50	NH NH _N NH ₂

ΓŞ

N NH F	N N NH	N NH
I-B-67	I-B-68	I-B-69
N-N-N-FF	I-B-71	I-B-72
I-B-73	I-B-74	I-B-75
N NH OH CI	I-B-77	N NH N NH I-B-78
I-B-79	N N N N N N N N N N N N N N N N N N N	S OH OH I-B-81

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N N N N N N N N N N		NH NH ₂
I-B-18	H OH N	NH OH Br
I-B-18	-он В 1-1	+ Q-o~Q B-190
S S S S S S S S S S S S S S S S S S S	I-B-193	1-B-194

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Applicants: Application No.:

I-B-237

I-B-238

I-B-239

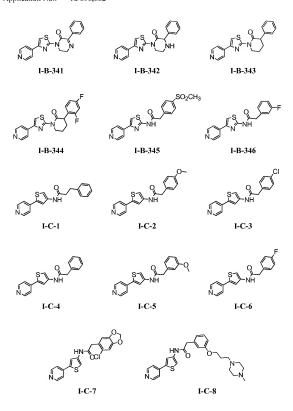
N= S-N- 1-B-240	I-B-241	1-B-242
1-B-243	I-B-244	1-B-245
1-B-246	I-B-247	I-B-248
S-NH CI	I-B-250	S NH Br

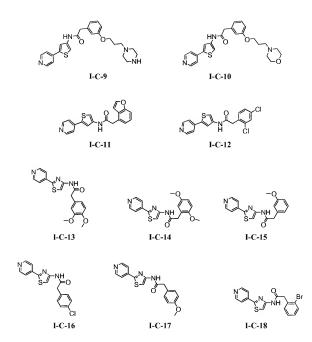
I-B-294

I-B-293

N I-B-	295	S F F I-B-296	S 0 0 0 0 1-B-297	
I-B-	9	I-B-299	S N F	
1-10-	230	1-0-277	1-13-300	
N S		I'S N F	S S S S S S S S S S S S S S S S S S S	
I-B-	301	I-B-302	I-B-303	
I-B-304 I-B-306				
N N	-S N N N N N N N N N N N N N N N N N N N	S NH	D-~~~	
	I-B-307		I-B-308	

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(Original) A composition comprising an effective amount of compound of claim
 and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

47-53. (Canceled)

54. (Currently amended) A method of treating or lessening the severity of a disease or disorder selected from glaucoma, Alzheimer's disease, an allergy, asthma, or diabetes in

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a patient, said method comprising administering to said patient a compound or a composition comprising a compound having the formula:

or a pharmaceutically acceptable salt thereof, wherein:

R1 is halogen, CN, NO2, or VmR;

 Z^1 and Z^3 are each independently CR^Z , and Z^2 is CR^1 ;

each occurrence of R^Z is independently halogen, CN, NO2, or U_nR ';

R2 is UnR';

X1 and X2 are each independently CR4 or N;

each occurrence of R4 is independently halogen, CN, NO2, or VmR;

each occurrence of U or V is independently an optionally substituted $C_{1.6}$ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by -NR-, -S-, -O-, -CS-, $-CO_2$ -, -COC-, -COC-, -COCO-, -CONR-, -NRCO-, $-NRCO_2$ -, $-SO_2$ NR-, $-NRSO_2$ -, -CONRNR-, -NRCONR-, -NROC-, -NRNR-, -NRSO-, or -SO-, or -SO-:

m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group; and each occurrence of R is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully

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unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or R and R, two occurrences of R, or two occurrences of R, are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

$$Q^1$$
 is -CO-, -SO₂-, or -SO₂NR-;
 R^3 is O^2 -Ar¹.

or R² and O¹-R³, taken together with the nitrogen atom, form the cyclic group:

, where s is 1 or 2, each occurrence of Y is independently, as valency and stability permit, -CO-, -CS-, -SO-, -O-, -S-, -NR⁵-, or -C(R⁵)₇-, and R⁵ is U.R':

 Q^2 and Q^3 are each independently a bond or a $C_{1.6}$ alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by -S-, -O-, -CS-, -CO₂-, -OCO-, -CO-, -CONR'-, -NR'CO₂-, -NR'CO₂-, -SO₂NR'-, -NR'SO₂-, -CONR'NR'-, -NR'CONR'-, -NR'NR'-, -NR'SO₂NR'-, -SO-, or -SO₂-; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of R^6 , wherein each occurrence of R^6 is independently halogen, CN, NO₂, or U_aR' , or two occurrences of R^6 , or R' and R^6 , taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; [[and]]

Ar¹ is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from oxygen or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from oxygen or sulfur; wherein Ar¹ is optionally substituted with 0-5 independent occurrences of TR⁷; wherein T is a

bond or is a C₁-C₆ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by –NR-, -S-, -O-, -CO₂-, -CO₂-, -COO-, -CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO₂-NR-, -SO-, or -SO-:

 ${\rm Ar}^2$ is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein ${\rm Ar}^2$ is optionally substituted with 0-5 independent occurrences of ${\rm TR}^7$; wherein T is a bond or is a ${\rm C}_1{\rm C}_6$ alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by ${\rm -NR}$ -, ${\rm -S}$ -, ${\rm -O}$ -, ${\rm -CS}$ -, ${\rm -CO}_2$ -, ${\rm -COCO}$ -,

-CO-, -COCO-, -CONR-, -NRCO-, -NRCO₂-, -SO₂NR-, -NRSO₂-, -CONRNR-,
-NRCONR-, -OCONR-, -NRNR-, -NRSO₂NR-, -SO-, or -SO₂-; [[and]]
each occurrence of R⁷ is independently R', halogen, NO₂, or CN; and
each of the optional substituents of said aryl or heteroaryl ring is selected from
halogen: -R°: -OR°: -SR°: phenyl optionally substituted with R°: -O(phenyl), optionally
substituted with R°: -(CH₂)_{1/2}(phenyl), optionally substituted with R°: -CH=CH(phenyl),
optionally substituted with R°: -NO₂; -CN; -N(R°)₂; -NR°C(O)R°; -NR°C(S)R°;
-NR°C(O)N(R°)₂; -NR°C(S)N(R°)₂; -NR°CO₂R°; -NR°NR°C(O)R°;
-NR°NR°C(O)N(R°)₃; -NR°NR°CO₂R°; -C(O)C(O)R°; -C(O)CH₂C(O)R°; -CO₂R°;
-C(O)R°; -C(S)R°; -C(O)N(R°)₂; -C(S)N(R°)₂; -OC(O)N(R°)₂; -OC(O)R°; -C(O)N(R°)₂;
-NR°SO₂R°; -N(OR°)R°; -S(O)₂R°; -SO₂N(R°)₂; -S(O)R°; -PO(R°)₂ -OPO(R°)₂;
-(CH₂)₂)NHC(O)R°; wherein each independent occurrence of R° is selected from
hydrogen, an optionally substituted C₁₋₆ aliphatic, an unsubstituted 5-6 membered
heteroaryl or heteroeyclic rine, phenyl, -O(phenyl), or -CH₂(fohenyl), wherein ontional

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substituents on the aliphatic group of R° are selected from NH₂, NH(C_{L-4}aliphatic), N(C_{L-4}aliphatic)₂, halogen, C_{L-4}aliphatic, OH, O(C_{L-4}aliphatic), NO₂, CN, CO₂H, CO₂(C_{L-4}aliphatic), O(haloC_{L-4} aliphatic), or haloC_{L-4}aliphatic, or two independent occurrences of R°, on the same substituent or different substituents, taken together with the atom(s) to which each R° group is bound, form a 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and

each of the optional substituents on said alkylidene chain, aliphatic, cycloalkyl, or heterocyclyl is selected from the list of optional substituents of optional substituents for aryl and heteroaryl rings and further comprise =O, =S, =NNHR*, =NN(R*)₂, =NNHC(O)R*, =NNHCO₂(alkyl), =NNHSO₂(alkyl), or =NR*, where each R* is independently selected from hydrogen or a C₁₋₆ aliphatic group.

- 55. (Previously presented) The method of claim 54, wherein said compound or composition is used to treat or lessen the severity of an allergy or asthma.
- (Previously presented) The method of claim 54, wherein said compound or composition is used to treat or lessen the severity of diabetes.
- (New) The method of claim 54, wherein said compound or composition is used to treat or lessen the severity of glaucoma.